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ANTIHYPOXIC AGENTS: LITERATURE SURVEY

Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 40, No 4, 1977 pp 504-509

[Article by V. S. Shashkov, G. S. Ratner and Ye. A. Kovalenko, Institute of Biomedical Problems, USSR Ministry of Health, Moscow, submitted 31 Aug 76]

[Text] The requirements of clinical and space medicine make it imperative to search for and investigate agents that attenuate the pathological influence of hypoxia.

Some authors (S. Ya. Arbuzov and L. V. Pastushenkov, 1969; P. V. Vasil'yev et al., 1971) divide antihypoxia agents into four groups: agents that augment the functions of physiological compensatory mechanisms; agents with depressive action; agents that affect cellular respiration and metabolism; agents referable to various pharmacological groups.

M. V. Korablev and P. I. Lukiyenko (1976) believe it expedient to divide antihypoxic agents into the following groups:

I. Agents that improve delivery of oxygen to tissues of the organism by means of: 1) increasing pulmonary ventilation, volumetric blood flow, amount of reticulocytes, erythrocytes and hemoglobin in peripheral blood; 2) increasing dissociation of oxyhemoglobin.

II. Agents that increase the resistance of organism tissues to oxygen deficiency by reducing expenditure of energy resources.

III. Agents that enhance energy production by means of: 1) correction of impaired tissular respiration, biological oxidation and oxidative phosphorylation; 2) increasing glycolytic activity.

IV. Agents that neutralize (decontaminate) the products of decompensated metabolic acidosis, normalize electrolyte metabolism and cell membrane function: 1) alkalizing agents; 2) agents that normalize potassium content of cells and ammonia metabolism; 3) agents that stabilize cell membranes.

For the sake of convenience of presentation, we deem it expedient to divide antihypoxic agents into two groups:

I. Agents that attenuate the sequelae of ischemia of vital organs (brain, heart) in the presence of circulatory hypoxia.

II. Agents that attenuate the effects of hypoxia induced by a shortage of oxygen in inspired air: 1) agents that attenuate the effects of hypoxia induced by lowered oxygen content of air (10-13%) and 2) agents that attenuate the effects of hypoxia induced by a low oxygen level in air (4-6%).

In spite of the fact that this division is arbitrary, such an approach is deemed to be justified for the following reasons. In the first place, the proposed classification makes it possible to describe, in a convenient form, the advances (quite modest thus far) in the field of searching for anti-hypoxic agents as related to the etiology of forms of hypoxia that are frequently encountered. The fact of the matter is that the mechanism of the deleterious effect of hypoxic hypoxia is appreciably different from the effect of circulatory hypoxia, since, in the latter instance, the organism is affected not only by the oxygen deficiency, but such factors as deficiency of nutrients, vitamins, enzymes, as well as accumulation of metabolic products. In the second place, the proposed classification enables us to explain, to some extent, some of the contradictory data in the literature pertaining to the effects of various products on hypoxia on the basis of differences in methods of creating hypoxic conditions and severity of hypoxia.

Many products have already been tested for antihypoxic agents. However, in this survey, we have referred only to the works, the authors of which succeeded in demonstrating a definite antihypoxic action of the tested products, as well as works containing contradictory data.

I. Agents That Attenuate the Sequelae of Ischemia of Vital Organs in the Presence of Circulatory Hypoxia

1. Surgery of vital organs (brain, heart), postinfarction states and other pathology leading to severe limitation of oxygen delivery to these organs are the most frequently encountered instances in clinical practice that require the use of drugs to attenuate the sequelae of hypoxia.

I. R. Petrov and V. A. Pukhov (1967) demonstrated the beneficial effect of a complex therapeutic agent on albino rats with ligated carotid arteries. Only 10% of the control animals survived, whereas this applied to 86% of the rats given a complex consisting of medinal, epinephrine, ACTH with inhalation of carbogen (2% CO₂). I. R. Petrov (1967) also established the efficacy of another complex of products, consisting of medinal [barbital sodium] (150 mg/kg), ethymizole (10 mg/kg), multiple vitamins (C, B₁, B₆ and others) and glucose. Preliminary administration of this complex resulted in survival of 90% of albino rats following ligation of both carotid arteries, over a 4-month observation period.

V. M. Vinogradov et al. (1968), who studied bioelectric activity of the cat brain following ligation of both carotid arteries and multiple administrations of potassium cyanide (KCN) in a dosage of 1 mg/kg, established that

KCN solution can be given 10-16 times with preliminary intravenous administration of 20-25 mg/kg hydroquinone. In control animals, bioelectric activity of the brain ceased after a single dose of KCN. However, hydroquinone is quite toxic: LD₅₀ constitutes 42-86 mg/kg for cats.

V. N. Belyy (1969) found that, while 48-hour survival of albino rats after ligation of common carotids did not exceed 22% in the control, it reached 50% after subcutaneous administration of 100 mg/kg gutimin (guanyltiourea) and 93% with administration of 10 mg/kg N-methylphenazine metasulfate.

According to the data of P. I. Likiyenko et al. (1971), fentanyl (0.5 mg/kg) and morphine (60 mg/kg) enhance survival of rats with cerebral ischemia, and fentanyl was 10 times more effective with regard to protection. According to the data of Benda et al. (1965), administration of segentin (phenylpropyl-diphenylpropylamine) to guinea pigs enhances retention of ATP in the myocardium in the presence of asphyxia: by the 5th min its level still constitutes 50.6%.

Belmonte and Monfort (1966) demonstrated a statistically reliable increase in survival time of albino rats (from 27.55 to 31.42 s) with administration of dipyridamole 30 min prior to drowning.

According to the data obtained by Rosner and Legros (1967) on cats with asphyxia, resistance of the cerebral cortex constitutes 97.9 ± 4.8 s and recovery time is 33.3 ± 6.2 s in the control, whereas the figures are 117.5 ± 6.1 and 23.7 ± 2.9 s, respectively, for animals given 16 mg/kg hydroxyl-chloroquine -chlorine-7[(N-ethyl-N-hydroxy-2-ethylamine)-4-methyl-1-butylamine]-4-quinoline--24 h prior to the experiment.

L. F. Rachinskiy (1974) made a comparative evaluation of the efficacy of antihypoxic agents in the presence of acute blood loss in experiments on dogs. Administration of gutimin, glucose-6-phosphate and cytochrome C in the presence of protracted (90 min) hypotension (40 mm Hg) increased 72-h survival to 50, 60 and 75%, versus 10% in the control.

II. Agents That Attenuate the Effect of Hypoxia Induced by Shortage of Oxygen in Inspired Air

1. Agents that attenuate the effects of hypoxia induced by lowered oxygen content of air (10-13%)

A reduction in oxygen content of the ambient atmosphere to 50% of the initial level is subjectively perceived by man, but at first the organism copes rather easily with such a shortage by virtue of compensatory mechanisms. However, a 50% reduction of oxygen content could lead to irreversible myocardial changes (within 72 h according to N. I. Gol'shteyn, 1941) and changes in the bodies of neurons of the cerebral cortex (Morrison, 1946). As established by Ye. A. Kovalenko et al. (1963), a reduction of oxygen level in inspired air to 10-15% leads to a drop of PO₂ to 74-48% in the cerebral cortex and 57-37% of the initial level in the subcortical layer, which could

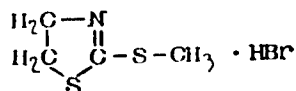
lead to impairment of brain functions. A 50% drop of PO_2 in the myocardium is critical, and this could be followed by ventricular fibrillation or cardiac arrest (V. B. Koziner and V. I. Korol'kov, 1968).

Thus, 10-13% oxygen in inspired air is, apparently, the borderline at which normal vital functions are still possible in man; at the same time, it should be borne in mind that prolonged exposure to such an atmosphere or further decrease in oxygen content could lead to serious consequences.

Mountain climbers could find themselves in such situations when they ascend to altitudes in excess of 6000 m without personal oxygen equipment, and this also applies to spacecraft and submarine crews in the case of malfunctions in the ventilation and oxygen supply systems.

Unfortunately, there are only isolated works dealing with the search for pharmacological agents that alleviate hypoxia under such conditions.

A. V. Pastushenkov (1969) discovered that meditan [structural formula given below] has a beneficial effect when given to rats, in a dosage of 50 mg/kg, 2 h before "climbing" to an altitude of 6000 m. At this altitude, control animals worked for 5 min, while those given this product worked for 9.9 min. The author also reports that central nervous system stimulants--phenamine, phenatine and caffeine--which increase oxygen uptake by brain tissues, either failed to demonstrate an effect or lowered efficiency.

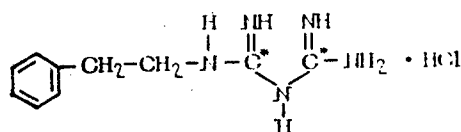


Meditan formula

Kronenberg and Cain (1968) investigated the effect of benzoic acid amide on 23 subjects who remained in an atmosphere with 12.4% oxygen for 72 h. The changes in physiological indices were indicative of faster adaptation of the respiratory system, while subjective sensations indicated that this agent alleviated acute decompression sickness.

Forwant et al. (1968) gave acetazolamide (diacarb, 2-acetylamino-1,3,4-thiadiazole-5-sulfonamide), in a dosage of 250 mg, to 43 subjects every 8 h before and 40 h after an experiment involving exposure to an atmosphere with 12.7% oxygen. The action of acetazolamide is based on its capacity to depress carbonic anhydrase activity and thereby lower the alkaline blood reserve. While control subjects developed moderate alkalosis and elevation of blood pH, which lasted for 8 h after the experiment, those given this product did not develop alkalosis and they tolerated better such symptoms of hypoxia as headache and insomnia.

In experiments conducted by Buckley et al. (1969) on albino rats, phenformin-HCl in a dosage of 75 mg/kg averted to a significant degree the effect of "high altitude" (5486-7135 m) on arterial pressure. The authors also found that, at an "altitude" of 6000 m, there were greater disturbances referable to trainability of rats than their endurance.



Phenformin formula

As demonstrated by P. V. Vasil'yev et al. (1971), in a dosage of 0.01 g, centedrin [meridil] normalized mental activity of subjects who breathed an artificial gas mixture with 10% oxygen 3 times for 50-60 min at 20-30 min intervals, when they breathed atmospheric air. A gas mixture containing 10% oxygen, 87% nitrogen and 3% carbon dioxide had a hypoxia-attenuating effect similar to that of centedrin. P. M. Gramenitskiy et al. (1955), Ye. A. Kovalenko (1965), I. R. Petrov (1967), V. B. Malkin and O. G. Gazenko (1969) demonstrated the desirability of adding carbon dioxide to inspired air in accordance with the extent of PO₂ drop.

V. V. Zakusov and R. U. Ostrovskaya (1971) demonstrated that diazepam (seduxen) has an antihypoxic effect in experiments on mice placed in a desiccator (up to 8.7 vol.% oxygen). Intraperitoneal injection of this agent to the animals, in a dosage of 10 mg/kg (1/24 LD₅₀) 30 min prior to putting them in the desiccator resulted in survival of the mice for 52±2.7 min, whereas the animals in the control group died within 23±1 min.

2. Agents that attenuate the effects of hypoxia induced by a low oxygen level in air (4-6%)

There may be a rapid drop in oxygen content of air, to 4-6 vol.%, as a result of breakdown of insulating outfits of individuals in various occupations--firemen, divers, mountain rescue workers, pilots, cosmonauts. Severe hypoxic disorders may be observed with this concentration of oxygen: excitement, EEG changes and, occasionally, convulsions [spasms] (Ye. A. Kovalenko and I. N. Chernyakov, 1972).

There are contradictory data concerning the effects of narcotics on hypoxia. On the one hand, they can lower oxygen intake by the organism due to the lower metabolic rate they induce. However, in the case of significant hypoxia of the organism, when oxygen uptake is already sharply reduced, narcotics have a toxic effect.

For example, G. A. Stepanskiy (1951) found that, of the three narcotics he tested (medinal, veronal, urethane), only the latter, in a dosage of 0.5 mg/kg,

elicited 80% survival of mice in a chamber with oxygen content of 5.5 vol.%. The survival rate of control mice constituted 14%.

The neuroleptic, aminazine, was used in the experiments of V. B. Malkin and Ye. V. Loginov (1968) and, in a dosage of 10 mg/kg, it lowered the resistance of mice and rats to acute hypoxia (4-6% oxygen in air).

A. V. Zelenchuk (1969) observed that a mixture of heparin (500 units/kg) and pipolphen (2.5 ml/kg), as well as heparin alone, had an antihypoxic effect. In the control, one-third of the rabbits survived 30-min exposure to an atmosphere with 6% oxygen, whereas in the group of rabbits given heparin (in the ear vein) all of the animals survived. In the case of 45-min exposure, 86% of the control animals died and this applied to only 8% of the rabbits given a mixture of heparin and pipolphen.

V. I. Sachkov et al. (1969) investigated the effects of new noninhalation anesthetics on the course of hypoxia. Mice kept in an atmosphere with 4.2 and 5.5% oxygen for 30 min were given oxybutyrate (500 mg/kg), viadril (50 ml/kg), hemineurine (160 mg/kg) and thiopental sodium (50 mg/kg) at different times 35-15 min prior to the experiment. In the control series, mean survival constituted 3.65 min and in the experimental ones, 7.65, 4.8 and 3.21 min, respectively. The survival rate among animals given oxybutyrate constituted 70% after the experiment (56.7% in the control group); the survival rate was lower among animals given other agents than in the control group.

The antihypoxic effect of GABA [γ -aminobutyric acid] derivatives is attributable to their sedative and narcotic properties, as well as the fact that GABA is the product of brain metabolism involved in processes of central inhibition. According to the data of S. V. Osipova et al. (1968), GABA derivatives increase the resistance of white mice to hypoxia by many times. With a mean pressure of 140 mm Hg in a pressure chamber, which corresponds to an oxygen content of about 4%, 77.3% of the animals died after 10-min exposure. Administration of γ -oxybutyric acid (GOBA) lowered the death rate to 8.3%, while administration of β -phenyl- γ -aminobutyric acid (BPGABA) lowered it to 16.7%. The authors report that the effect of BPGABA lasts twice as long as that of GABA, but the former is five times more toxic.

According to the data of Wilhjelm (1966) survival time of mice exposed to an atmosphere with 5% oxygen increased from 3.1 to 7.9 min after intake of thiopental sodium.

Antioxidants and radioprotectors similar to them in mechanism of action have some antihypoxic effect. V. I. Generalov (1968) established that some radioprotectors (cystamine, tetramethylcystamine), in a dosage of 50-150 mg/kg, may have a negligible attenuating effect on hypoxia, and this applies in particular to experiments with tetramethylcystamine on mice. At the same time, the earlier studies of P. G. Zherebchenko (1965), referable to radioprotectors in the indolylalkylamine group and some other agents (tryptamine, hydroxytryptophan), demonstrated that these agents have an adverse effect in the presence of hypoxia.

In studies of some antioxidants (Ye. Ya. Kaplan and V. V. Ogleznev, 1968), the best results were obtained with mexamine (200 mg/kg) by mouth. These agents elicited a 1.5-fold prolongation of survival time, as compared to the control.

As indicated by R. P. Simorot and P. I. Lukiyenko (1966), vinyl compounds (vinylsulfones, vinylsulfoxides and vinylsulfides) protect mice from death in the case of 15-min exposure to an "altitude" of 10,500 m (~5% oxygen). Evidently, the antihypoxic effect of these agents is based on blocking of free oxidation, since they inhibit cytochromoxidase. Unfortunately, the authors do not quote absolute figures with regard to prolongation of survival after administration of these agents.

In the experiments of G. I. Gurvich and K. S. Shadurskiy (1963) on guinea pigs, white mice and rats, a record was kept of the time of respiratory arrest following an "ascent" to an "altitude" of 11,000 m (4.7% oxygen). While control animals survived for 0.2-16 min, experimental ones, which were given serotonin (0.2 mg/kg intramuscularly) 1 h before the "climb" survived for 1.8-60 min. As we know, serotonin elicits contraction of smooth muscles of internal organs and constriction of blood vessels. Perhaps, the antihypoxic effect of serotonin was attributable to better blood supply to the brain due to redistribution of blood in the organism.

P. I. Lukiyenko (1968) studies several agents in experiments on mice placed in closed containers without carbon dioxide in one instance and in a pressure chamber with 4.9% oxygen, in the presence of hypocapnia, in another. While control animals survived for up to 30 min in the closed containers ("vessels"), animals given the cholinomimetics, pilocarpine, proserine [neostigmine] and acetylcholine, 15 min before the experiment survived for 70, 55 and 42 min, respectively. Proserine was found to be the most effective in the case of hypoxia associated with hypocapnia. The peripheral cholinolytic atropine, adrenolytics and the sympatholytic octadin lowered resistance to hypoxia.

S. V. Osipova (1968), who studied analeptics, found that corazole had a mild protective effect on hypoxia in the presence of 6% oxygen. In the control, 64 out of 67 animals died after 10-min exposure. Albino rats given 40 mg/kg corazole had a better survival rate (7 out of 10, 3 out of 10 and 2 out of 20). Cordiamine did not have a protective effect.

Intraabdominal administration of lactic or hydrochloric acid to mice, at the rate of 0.4 ml/10 g mass (pH 2.4, concentration 0.1-0.5 and 0.005 N), prolonged survival of animals in an atmosphere with up to 2.5% oxygen. Control animals lived for 3-4 min and experimental ones, 9-10.5 min (A. Kh. Kogan et al., 1969), and this is perhaps attributable to reduction of alkalosis induced by hypoxia.

Powell and Buckley (1968) put rats in a chamber with 6.1% oxygen for 1 h, 5 days a week. In the control, 50% of the animals died, whereas all of the animals in the group given 75 mg/kg phenformin-HCl survived.

According to the data of Cheymol et al. (1964), albino rats kept in an environment with 4% oxygen survived for 7 to 23.5 min. Administration of catalase (5000 units/kg) and lipoxidase (125 mg/kg) 3 h before the experiment increased survival time to 18-88 min.

P. I. Lukiyenko (1973) tested the effect of macroergic compounds (ATP, ADP, AMP) and adenosine on mice with the animals "lifted" in a pressure chamber to an "altitude" of 10,700 m (179 mm Hg) and placed in an airtight 250-ml vessel without CO₂ absorption. Subcutaneous administration of these agents in doses of 200, 150, 128 and 82 mg/kg, respectively, elicited survival of all animals for 15 min at an "altitude" of 10,700 m; all of the control animals died. In the sealed area, animals given these agents lived 2.5-4 times longer than controls (for 130 and 35 min, respectively). The author voices the opinion that macroergic phosphates accelerate utilization of oxygen in the brain, without affecting skeletal muscles.

According to the data of A. V. Piskarev et al. (1973), of the pyrazolone and hydrazine derivatives they studied, only one agent in the hydrazine class, apressin, had a mild antihypoxic effect in experiments on mice ("climb" to 10,000 m altitude).

L. A. Annaurova (1974) tested the effect of nerobol on young (120-140 g) albino rats exposed to an "altitude" of 7000 m for a long time (6-12 h daily for 30 days). Nerobol eliminated the inhibitory effect of hypoxia on animal growth only when they were exposed to a low PO₂ for no more than 6 h per day.

A. S. Zakharevskiy et al. (1976) studied the effect of amichlophen (para-chlorophenoxyacetic acid diethylaminoethylamide) given intraperitoneally in a dosage equaling $\frac{1}{9}$ LD₅₀ 60 min before putting the animals in a pressure chamber (198 mm Hg for 2 h). This agent increased the energetic efficiency of respiration and stabilized the membranes of cell organelles.

Conclusion

On the basis of the submitted material, it can be concluded that we still do not have reliable agents that would attenuate appreciably and for a long time the effects of hypoxia of the most diverse etiology and severity. However, some of the studies, although conducted primarily on animals, do prove that it is basically possible to control hypoxia by means of therapeutic agents.

M. V. Korablev and P. I. Lukiyenko (1976) believe, on the basis of the results of their own research and data in the literature, that it would be purposeful to search for new antihypoxic agents among adenine nucleotides and adenine-dinucleotides, enzymes of biological oxidation, amino acids, sulfhydryl group donors, derivatives of adenine, hydrazinephthalazine and phenothiazine, since these agents have a marked antihypoxic effect on various forms of hypoxia. The authors deem it useful to continue clinical investigations of cytochrome C,

ATP, NAD, NADP, glutamic and ascorbic acids, methionine, tryptophan, cysteine, glutathione, dicapitol, dimedrol [benadryl], diprazin [promethazine], sodium oxybutyrate, fentanyl, apressin, gutimin and other agents.

Apparently, GOBA and some GABA derivatives are the preferred antihypoxic agents at this time.

In conclusion, we must voice some considerations concerning the directions to be pursued in searching for drugs that attenuate the effects of hypoxia on the organism.

In the presence of hypoxia, the primary disturbances of morphological structure of various organs refer primarily to mitochondria and cell membranes (Ye. F. Kotovskiy and L. L. Shimkevich, 1971). In this case, a search for appropriate agents and investigation of the mechanism of their action, directed toward preserving the activity of cell membranes and mitochondria in the presence of hypoxia, could be a fruitful direction for pharmacologists and biochemists.

Investigation and research referable to agents that help retain ATP may be one of the possible avenues in this direction (D. L. Ferdman and P. D. Dvornikova, 1940) and, on the other hand, this applies to agents that dissociate oxidation and phosphorylation under certain conditions (V. P. Skulachev, 1964); it may also be interesting to find pharmacological agents that would permit temporary and selective dissociation of lipid-protein complexes that make up the cell membranes (K. G. Manukyan, 1964; I. N. Ulybina and D. A. Chetverikov, 1966; N. S. Gel'man, 1967; Shtraub, 1963), which play an enormous role in central nervous system function.

At the same time, it should be assumed that only a complex of agents, each of which acts on a specific level of the organism, would yield an adequate antihypoxic effect.

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PHYSIOLOGY

DYNAMIC SPEECH SPECTRUM ANALYZER

Frunze IZVESTIYA AKADEMII NAUK KIRGIZSKOY SSR in Russian No 3, 1977 pp 91-95

[Article by N. V. Andreyeva, E. B. Donbayev, Ye. K. Kashayev, and B. V. Pospelov]

[Text] The speech spectrum analyzer is one of the main instruments used in speech research and, in particular, linguistic research. Because the requirements imposed on speech spectrum analyzers are rather specific and their production has not yet been organized, the problem of developing, planning, and manufacturing these instruments on the basis of individual orders is becoming very pressing.

The dynamic spectrum analyzer of speech signals described below is intended for operation in laboratories of experimental linguistics, and it has the following basic characteristics: Range of analyzed frequencies--50-12,000 Hz; number of spectrum channels--50; the distribution of the middle frequencies of the filter channels corresponds approximately to the Koenig scale; the amplitude-frequency characteristics of the individual filters is a second-order frequency-selective factor; a linear detector allows for a dynamic range of not less than 50 db and simultaneous integration with a time constant on the order of 10 msec; the commutator sweep cycle length is 15 msec; the analyzer as a whole allows for a dynamic working range of not less than 40 db; there is a possibility for frequency correction of an input signal with a tendency of +6 db/octave; the output signal can be observed on both linear and logarithmic scales, and it can be recorded on motion picture film when the appropriate attachment is available.

The analyzer's structural diagram includes an input unit and a spectrum channel unit containing the commutator switches which are controlled by timer pulses having a repetition frequency of 67 Hz. The succession of AM pulses from the commutator outputs is combined in the output unit, and after appropriate conversion they can be fed to a recording block controlled by timer signals.

The input unit preamplifies the input signal, its frequency characteristic, and a power-corrected spectrum channel unit matching signal. In addition

the input unit permits monitoring of the analyzer's efficiency, both in individual channels and as an entire unit. A monitoring signal with a known filter can be fed to the analyzer input in the monitoring mode.

The spectrum channel unit contains 50 channels of the same kind, covering a frequency range from about 50 to 12,000 Hz. Each channel has a band filter, a linear detector, an integrator, and a commutator switch. The channels differ from one another in relation to the frequencies to which the filters are tuned and their passbands.

Complying with the technical requirements, the distribution of the resonant frequencies of the filters and their passbands in relation to the frequency range corresponds on the average to the distribution adopted for the Spektr-2 system (1). The distribution of the resonant frequencies of filters in the variation range of each of the first three formants was selected to be uniform in order to facilitate filter tuning and make the analyzer's channels more identical. The filter bandwidth of each of these ranges is approximately constant. In the frequency range above 3,500 Hz the resonant frequencies are distributed according to a stepped interval expansion law. The same pertains to the distribution of the widths of the filter passbands.

The entire high frequency range is arbitrarily divided into three subranges corresponding to the three high frequency formants-- F_4 , F_5 , F_6 .

The table below shows data on the distribution of the resonant frequencies of the filters and the boundaries of their passbands. For the purposes of comparison the second column shows the distribution of resonant frequencies adopted for the Spektr-2 system.

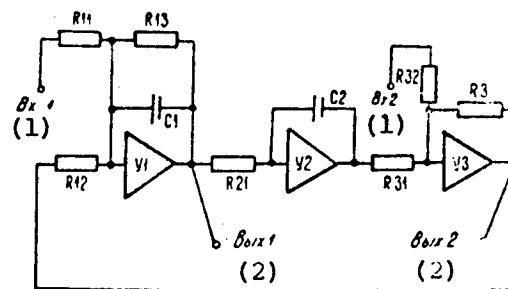


Figure 1

Key:

1. Input

2. Output

The band filter is a circuit based on an active second-order RC -selective factor, which has a number of significant advantages over passive LC -factors (2,3). Its transfer characteristic has the form:

$$W = Dp / (p^2 + Ap + B).$$

№	(1) $t_0, \tau u, \text{Спектр}$	(2) $t_0, \tau u$	$\Delta t, \tau u$	$t_H, \tau u$	$t_0, \tau u$	•
1	160	100	100	50	150	$\leftarrow F_0$
2	277	200	100	150	250	
3	395	300	100	250	350	F_1
4	512	400	100	350	450	
5	630	500	100	450	550	
6	750	600	100	550	650	
7	867	700	100	650	750	
8	987	800	100	750	850	
9	1105	910	120	850	970	F_2
10	1225	1030	120	970	1090	
11	1347	1150	120	1090	1210	
12	1465	1270	120	1210	1330	
13	1535	1390	120	1330	1450	
14	1707	1510	120	1450	1570	
15	1830	1630	120	1570	1690	
16	1953	1750	120	1690	1810	
17	2080	1870	120	1810	1930	
18	2207	1990	120	1930	2050	
19	2335	2110	120	2050	2170	
20	2465	2245	150	2170	2320	E_3
21	2598	2395	150	2320	2470	
22	2732	2545	150	2470	2620	
23	2867	2695	150	2620	2770	
24	3010	2845	150	2770	2920	
25	3150	2995	150	2920	3070	
26	3293	3145	150	3070	3220	
27	3450	3295	150	3220	3370	
28	3605	3445	150	3370	3520	
29	3766	3600	160	3520	3680	F_4
30	3934	3765	170	3680	3850	
31	4110	3940	180	3850	4030	
32	4295	4125	190	4030	4220	
33	4490	4320	200	4220	4420	
34	4700	4525	210	4420	4630	
35	4915	4740	220	4630	4850	
36	5140	4965	230	4850	5080	
37	5390	5205	250	5080	5330	F_5
38	5650	5465	270	5330	5600	
39	5930	5745	290	5600	5890	
40	6240	6045	310	5890	6200	
41	6560	6365	330	6200	6530	
42	6910	6705	350	6530	6880	
43	7300	7065	370	6880	7250	
44	7730	7445	390	7250	7640	
45	8176	7845	410	7640	8050	
46	8700	8310	520	8050	8570	F_6
47	9260	8890	640	8570	9210	
48	9870	9590	760	9210	9970	
49	10550	10410	880	9970	10850	
50	11294	11350	1000	10850	11850	

Key:

1. Hz, Спектр

2. Hz

A circuit with three operational amplifiers can serve as an example (Figure 1). The analyzer filters are designed on the basis of known coefficients A , B , and D of the transfer function. An equation system is written to determine the components of the circuit. Inasmuch as the number of unknowns is greater than the number of equations, certain components must be assigned beforehand. We usually select

$$C_1 = C_2 = C_p; R_{13} = R_{\Delta}; R_3 = R_{31} = 10 \kappa; R_{12} = R_{21} = R_p.$$

What remains to be computed are resistances R_p and R_{Δ} , which correspondingly define the filter's resonant frequency and passband width:

$$R_p = 1/\omega_p \cdot C_p = 1/2\pi \cdot f_p \cdot C_p;$$

$$R_{\Delta} = 1/\Delta\omega \cdot C_p = 1/2\pi \cdot \Delta f \cdot C_p;$$

where f_p is the resonant frequency and Δf is the filter's passband width, the values of which are taken from the table.

The size of C_p is selected in such a way as to insure the necessary reactance at the filter's resonant frequency. The instability of the temperature, tuning frequency, and passband of the examined filters, which are based on 1UT401B operational amplifiers, does not exceed 1 percent. Instability of the transmission factor is compensated for by adjustment of R_{11} . Repeatability of the filter amplitude-frequency characteristics can be insured by using resistors R_{12} , R_{13} , and R_{21} with a deviation of ± 0.5 percent. Figure 2 shows an example of an amplitude-frequency characteristic with $f_p = 600$ Hz at a bandwidth $\Delta f = 100$ Hz, measured at an intensity of 0.7.

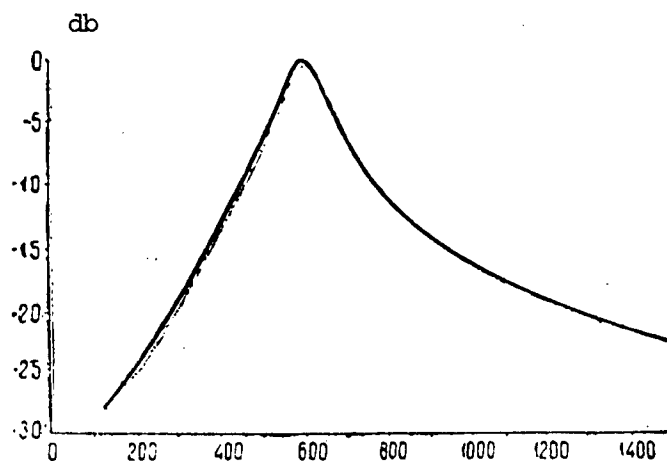


Figure 2

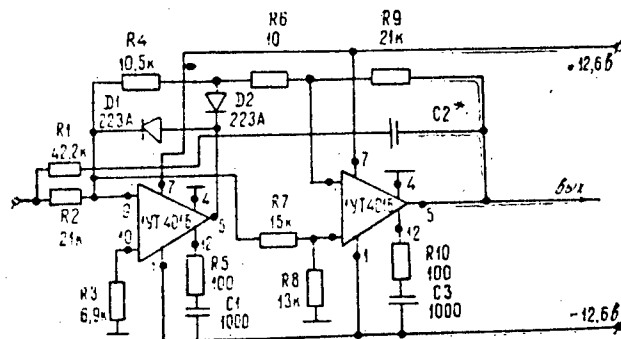


Figure 3

The second basic unit of the analyzer's spectrum channel is the linear detector. The main requirement imposed on this unit is that it must allow a dynamic working range of not less than 50 db. Figure 3 shows a simplified basic electric circuit of the detector and an integrator. The first 1UT401B microcircuit works as a half-wave rectifier and the second works as an input and output signal summator. The output voltage of the first cascade is zero for a negative input signal due to addition of diode $\Pi 1$ in a feedback circuit. In this case the second microcircuit works as an inversion amplifier with an amplification factor $k_1 = -R_9/R_1$. When a positive input signal is involved the first cascade works as an inversion amplifier with an amplification factor $k_2 = -R_4/R_2$, while the second works as a summator:

$$U_{out} = U_{in} (\kappa_2 \cdot \kappa_3 + \kappa_1), \quad \kappa_3 = R_9/R_6; \quad \kappa_1 = \kappa_2 = -0.5.$$

The output voltage is positive in sign. The integrator consists of the circuit $C_2 \cdot R_9$, which has a time constant $\tau = 10$ msec. Resistors R_1 , R_2 , R_3 , R_4 , R_6 , and R_9 must be chosen with a deviation of ± 0.5 percent so that the amplitude characteristic would have the necessary shape.

The electronic commutator is a system of switches based on KP-305D field transistors controlled by timer signals, which successively sweep the spectral cross section in time with a 15 msec cycle. In their initial position, all switches are kept closed by a positive voltage from the divider output. This is why a zero potential exists at the output. When a negative pulse comes from the timer the appropriate switch assumes its saturated state for the time of action of the test signal. During this time the voltage passes from the detector's output to the output with a transmission factor defined by parallel connection of the resistors of the remaining (closed) channels. Thus the pulse at the summator output would have an amplitude proportional to the speech envelope within the band of the corresponding channel. In view of the detector's low output resistance the spectrum channel unit is well matched with the commutator, making it possible for the spectrum channel to work at a low-ohmic load.

The timer produces a succession of test pulses at an interval of 30 μ sec distributed in space among 50 separate outputs. Moreover it produces a reference pulse and a cycle start marker, which can be used simultaneously to start a movie camera and control the sweep of an oscillograph. The timer has a standard "traveling unit" circuit assembled on the component chassis of an Ural-14 computer complex. It includes an advancing pulse oscillator, a matching device, a "traveling unit" circuit, and units producing the cycle synchronization marker and the reference signal. When necessary the timer can be transferred to any other component chassis intended for discrete (IMS).

The output unit is intended for summation of the signals of the commutator and timer as well as for their amplification in a linear or logarithmic scale. The summator is a sufficiently low resistor, the resistance of which is defined by the loading capability of the detector (100-200 ohms). The signal passes from the summator output to the inputs of the linear and logarithmic amplifiers. The analyzer can be set in two working modes by means of a switch--linear and logarithmic. The input signal is fed to the vertical deflecting plate of an oscillograph (S1-16, S1-19) so that it could be observed; a sweep voltage synchronous with the cyclic frequency of the electronic commutator is fed to the horizontal plate.

The output signal can be recorded by a motion picture attachment using 16-mm movie film.

The camera's working speed is synchronized with the commutator cycle synchronization marker, synphasally with the sweep of the electronic oscillograph. When a two-dimensional spectrum must be recorded a loop oscillograph can be used, for which purpose the analyzer must be outfitted with a direct current power amplifier.

This variant of the spectrum analyzer was introduced at the Moscow State Pedagogical Institute of Foreign Languages imeni M. Torez and at the Institute of the Countries of Asia and Africa of Moscow State University. It is used in speech research in laboratories of experimental phonetics. Utilization of the advantages of unified circuit concepts and of a modern component chassis has resulted in a dynamic speech spectrum analyzer satisfying the requirements presently imposed on such devices.

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PSYCHOLOGY

PREDICTION OF FLIGHT SKILLS

Moscow AVIATSIYA I KOSMONAVTIKA in Russian No 9, 1977 p 22

[Article by Engr-Lt Col A. Vetokhov, Cand Psych Sci]

[Text] The quality of the retraining airmen learning to operate new equipment experience depends on the firmness of the theoretical knowledge they had acquired in aviation disciplines and their ability to perform practical exercises of varying complexity. This is why sensible distribution of the available time for acquisition of knowledge and skills is one of the major problems of the training process.

Practice shows that skill development can be predicted with a consideration for the individual features of the students, since this process follows an exponential law. As the number of exercises increases the time spent on their fulfillment decreases, with the number of permissible errors decreasing concurrently as well. After a certain number of exercises the students become "saturated" with knowledge and skills. This exponential curve has come to be called the exercise curve in pilot training (see figure).

By evaluating training progress on the basis of this exponential curve we can determine the number of exercises necessary for acquisition of sound knowledge. The exponential curve, which is plotted from experimental data, also serves as an objective quantitative characteristic of the results of the search for new, more-effective airman training procedures and methods.

If the procedures being practiced are discrete, for example those of checking the operability of apparatus, searching for and turning on the required tumbler switch, or setting the readings of a particular instrument, then the exercise curve is plotted on the basis of the data acquired during training, and it then represents a functional dependence between the number of errors and the number of exercises.

But when the skills of nondiscrete actions are involved (for example those of tracking a target), the instructor notes down the target tracking time and the size and number of tracking errors. Using them, after computing the mean target tracking error he plots the exercise curves, which now express the dependence of these variables on the number of exercises (n).

[Graph not reproducible]

Exercise (Exponential) Curve: $t_{set\ ave.}$ --Average maximum exercise completion time obtained by averaging the re-training (training) results of previous flight groups; τ --exercise curve constant (projection of the segment of the tangent to the exponential curve, drawn from the coordinate origin to line $t_{set\ ave.}$, onto axis n); n_{set} --number of exercises required to produce a given training level t_g for the given student. As an example, $n_{set} \approx 3\tau$ when $t_g = 0.95 t_{set\ ave.}$.

Key:

- | | |
|--|-----------------------------|
| 1. Exercise (exponential) curve | 4. Tangent |
| 2. $t_{set\ ave.}$ | 5. n_{set} |
| 3. Exercise completion time, t , sec | 6. Number of exercises, n |
| | 7. t_g |

The exercise curve, which reflects the dependence of the time required to complete the first exercises on the number of times they are repeated, tells the instructor a great deal. As an example it provides information on the progress the student is making in developing his skills and, consequently, on the nature of the differential approach required to his training.

However, such curves do not provide information on the effectiveness of the training methods, and it is difficult to use them to predict the needed number of exercises for complete skill development. For this purpose, when retraining pilots, as an example from an airplane (helicopter) of one type to another, we determine the average maximum time required to complete a particular exercise ($t_{set\ ave.}$), the average permissible number of errors, and so on. In other words we establish standard levels for different training level characteristics, which would then allow the instructor to plot exercise curves for each student with just the first three exercises and predict, on their basis, the additional number of exercises required when retraining other similar flight groups.

After plotting $t_{set\ ave.}$, the three experimental points on the exponential curve representing its initial segment, and the tangent to this curve from the coordinate origin until its intersection with the training level line $t_{set\ ave.}$, the instructor determines τ and then $n_{set} \approx 3\tau$ --that is, the number of exercises required by the given student. Thus when $t_{set\ ave.}$ is known the instructor's determination of the required number of exercises boils down to plotting three points, drawing the initial segment of the exponential curve and the tangent, and determining τ and n_{set} .

This graph can also be used to determine n_{set} for other students in the group. A dramatic difference between n_{set} and $n_{set\ ave.}$ (obtained from the averaged curve for similar groups which had undergone retraining earlier) would indicate that the training procedure employed with the particular student should be changed and that more attention must be devoted to this student.

There is another possible approach to using the exercise curve. By plotting many curves representing retraining of previous groups we determine the limits of the normal trend in practical training. Exercise curves plotted during the current retraining session permit the instructor to reveal the swiftness with which skills are acquired and the number of exercises required, and to determine which airmen are exhibiting training progress outside the set limits.

Thus the time required to acquire knowledge and develop stable skills can be predicted, making it possible to use an individual approach in airman training.

In our opinion use of the proposed method will promote higher quality and a reduction in the time required to retrain flight personnel for new equipment.

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PSYCHOLOGY

MENTAL FLIGHT MODEL

Moscow AVIATSIYA I KOSMONAVTIKA in Russian No 9, 1977 pp 20-21

[Article by Asst Prof, Cand Psych Sci, Engr-Col R. Rubin and Physician-Pilot Cand Med Sci Lt Col V. Kuznetsov]

[Text] Senior Lieutenant A. Antipov faced a difficult test on this overcast day--intercepting an airborne target aboard a new fighter and landing at minimum visibility. The airplane took off, disappearing into the clouds in no time at all. The pilot's mood was excellent: His craft climbed obediently. He was soon greeted by the Sun. The terse, sharp commands of the fighter controller were answered by the pilot's actions with no less efficiency. An attack, and the target was knocked down.

Reporting completion of his assignment Antipov turned his airplane in the direction of the airfield and, on instructions from the command post, began his descent. It became dark in the cockpit. Unbroken clouds engulfed the airplane. The pilot riveted all of his attention to his descent. The scale of the course indicator began to gradually stray to the left. Could the course system possibly have failed? The artificial horizon told him that the airplane was not banking. But the pointer of the turn indicator was almost all the way to the right. This had to mean that the craft was in fact banking! The pilot had to immediately determine which of the instruments had failed.

Antipov smoothly moved the airplane's control stick left. The pointer of the turn indicator approached the zero mark, and the scale of the course system stopped moving. But the artificial horizon began to indicate a 35° left bank. Clearly the artificial horizon had failed. The pilot reported the incident to the flight leader. In response he heard the command: "Relax. Fly with the back-up instruments."

The pilot focused all of his attention on them. He had to shut his mind off from the artificial horizon. But this was not so simple. Practiced to the point where they were automatic, the habits of distributing and switching attention now seemed to interfere with the pilot. His gaze continued to return to the artificial horizon, and the control stick kept

deflecting right as if it had a mind of its own, counteracting the fictitious bank.

The altimeter's pointer indicated a continuous drop in altitude--1,000, 800, 500 meters. It became lighter. Finally the ground could be seen through breaks in the clouds. But the landing strip was not yet to be seen, though soon he could hear the long-range homing signal. The bell of the radio beacon sounded. The pointer of the automatic radio compass shuddered and once again stopped at zero. In a little bit the landing strip could be distinctly seen. The young pilot had honorably completed his difficult test: While in the air he had come across a situation that drastically altered the structure of his perception and processing of instrument information, owing to which the pilot's mental flight image underwent distortion.

We recalled this incident on reading the responses to the article "Mental Flight Image" by Engineer-Major General Yu. Dobrolenskiy and Colonel Medical Service V. Ponomarenko. We believe that discussion of this subject in this journal is extremely important and useful. The debate touches upon important problems in flying skill and flight safety. We would now like to state our opinion.

We know that instrument flying is one of the complex elements of combat training requiring active intellectual activity on the part of the pilot directed at determining the airplane's position in space. Through sensations, perceptions, memory retrieval, and complex mental processes--information analysis, synthesis, and decoding--the pilot achieves a generalized visual flight image or, as it is commonly called in air engineering psychology, a conceptual (mental) flight model.

In the air, the pilot makes use of operational images that are a part of the mental model of the concrete flight. The principal quality of an operational image is its mobility, the variations it experiences during piloting depending on the arising conditions. Formation of a conceptual model and operational images of the flight depends not only on the pilot's training level and experience but also on the volume and nature of the information he perceives.

The sum total of information permitting the pilot to assess the airplane's position in space, the parameters of its movement, and the working conditions of various systems is commonly called the information model or instrument analog of the flight. Using it, depending on the nature and goal of the assignment the pilot stabilizes the flight parameters or changes them according to particular laws. In other words in instrument flying the pilot interacts in a sense not with the airplane but rather with its analog--the information model of the flight. In this case he is deprived of the possibility for directly observing the object of control or the correctness of his control actions. As a result of perceiving and processing the instrument information the pilot develops a mental model of the flight and operational images, comparison of which with the information model permits him to determine the extent to which that which is expected matches that which

exists in reality, and it permits him to continue to control the airplane with a consideration for the real situation and the predicted future.

However, the information model contains not only instrument signals but also other factors affecting the pilot--accelerations, vibrations, and the sound of the working engine. Although in a number of cases they carry a great deal of information, they nevertheless may distort the flight image, leading to illusory perception of spatial position. Instruments are the main sources of information.

We know from practical experience that when shortcomings arise in the flight information model, as had occurred with Antipov when his artificial horizon failed, the mental model experiences distortion, and this leads to change in sensomotor activity. Thus the change which occurred in the information model prevented the young pilot from immediately determining the cause of the evolved situation. Thus he was forced to alter his pattern and seek the necessary information. In this case the dynamics of the search for the failed instrument involved formation of operational images and their comparison with the expected flight image. Meanwhile the grounds upon which decisions were made was the newly formed image of the evolved situation--that is, the operational mental flight model. During subsequent descent the shortcomings of the information model resulted in a change in the stereotype of information perception and provoked the pilot's impulsive actions to counteract a false bank, making it difficult for him to maintain the required flight conditions.

It may be argued that these premises are typical of only manual instrument piloting. It would appear that the pilot would require less of a visual impression of the flight in semiautomatic and automatic control using integrated navigational systems. Unfortunately we still encounter such assertions in practice. Some young pilots who have mastered airplanes having automated and automatic control systems subconsciously decrease their attention to monitoring general piloting and navigational information in trying to quickly master the skills of flying in director and automatic control modes. They in a sense constrict their intellectual activity directed at forming the flight image, reducing it in semiautomatic mode to just responses to command signals and, in automatic mode, to monitoring instrument readings. This could lead to a loss of the habits of mental generalization of piloting and navigational information and, in the end, to undesirable consequences. This phenomenon is usually observed among passive pilots who try to lighten their load excessively with the assistance of automatic systems.

Now that modern airplanes are equipped with automatic and semiautomatic control systems, significant changes have occurred in flight psychology. Thus inclusion of a computer in the "pilot-airplane" control loop to produce piloting and navigational information and to shape the command signals has relieved the pilot of the need to create complex operational images, and it has simplified the control movements. A simplified operational image created on the basis of command information--that is, the positions of the

indicators--has become the "triggering signal" in piloting. Meanwhile positional information, which characterizes the spatial position of the airplane and which is extremely important to flight safety, has in a sense become secondary. As a result during his control of the aircraft the pilot may move controls without thinking; this would mean that he may not always recognize the end goal of his actions completely and fail to monitor the airplane's position in space. In semiautomatic mode, command information in a sense screens off instrument information, resulting in formation of simplified operational images and thus reducing the significance of the generalized flight image. Thus a very important detail of pilot activity--the "feel of the airplane"--is diminished in importance.

The psychological structure of pilot activity changes even more with automatic piloting. Control movements are excluded from the sensomotor process in this mode, as a result of which motor information is dropped from the perception system; playing a feedback role, this information has great significance to development of a "feel of the airplane" and, consequently, the flight image.

Research has shown that when the pilot is insufficiently trained and experienced these features place a certain imprint upon his behavior in response to unforeseen changes in the flight conditions. As an example the same pilot working with a flight trainer would require more time to detect failure of the artificial horizon in semiautomatic mode than in manual mode. This law is also observed when failures of other instruments and machine units, including the computer or the command-piloting instrument, are simulated.

Flying practice and the research that has been performed show that exercises in flight trainers in which failures of automatic resources are simulated are an effective part of flight crew lessons. Moreover experience shows that it is best to simulate such "failures" at the very beginning of the training, informing the pilot of this beforehand and thus creating a particular psychological set within him. The instructor should help the pilot reveal the dependence in the created situation between the information model and the real and formed flight images. Using such trainers, pilots not only assimilate the signs of failures but also learn to efficiently analyze their manifestations by establishing the mutual relationship between the basic and command information. They become convinced of the need for actively forming the flight image, and they acquire the habits of piloting in combination with monitoring spatial position more effectively.

All of this pertains in our opinion to the navigational component of the flight model as well. Modern navigational systems make it possible to automatically solve the basic problems of navigation--determining the airplane's current coordinates and the flight conditions at a given point. In order to form the navigational component, as he perceives the current information the pilot must know how to mentally reckon his course, continually determining the location of the airplane and maintaining a clear impression of the flight conditions that should be maintained.

The following question naturally arises. Is creation of a flight image only the consequence of direct sensations and perceptions and subsequent information processing? We believe not. The problem is that formation of the flight image is governed not only by sensations, perceptions, and thinking, but it is also a consequence of memory retrieval--reproduction of that which had been perceived earlier. In flying practice, where activity involves significant participation of the first signaling system, the impressions produced may be sufficiently complete and stable, though of course depending on the pilot's experience and individual features. Moreover the pilot's orientation toward determination of particular flight elements, achieved through perception, has a great influence on the nature of the reproduced images. Thus during preflight preparations, while thinking out the assignment, the impressions arising in the pilot (especially an experienced pilot), in a sense as conditioned reflex reactions, may elicit so-called ideomotor acts--slight contractions of eye muscles and barely noticeable hand movements.

Considering the psychological features of pilot activity examined above, we believe that the wording suggested by Major General Yu. Dobrolenskiy and Colonel Medical Service V. Ponomarenko--"A flight image is an impression of the flight continually created by the pilot as he flies on the basis of acquired experience and the effects of all sources of information"--requires elaboration. In the first place the definition does not include important cognitive processes such as sensation, perception, memory, and thinking, nor does it consider the pilot's intellectual capabilities. Second, the assertion of the authors that the flight image is continuous is not undebatable.

Thus the "flight image" concept plays a great role both in flying practice and in creation of more-sophisticated piloting and navigational indicator systems. At the same time a distinct definition of this concept does not as yet exist in the specialized literature. Wording this definition is an extremely complex task. We will apparently be able to do so after we summarize the discussion, after various specialists state their opinions on the meaning of the issue raised.

The wording we suggest is: "A flight image is a mental flight model formed as necessary in the pilot's consciousness as a result of cognitive mental processes (sensation, perception, memory, and thinking) on the basis of experience, knowledge, habits, and skills, with a consideration for the individual psychological features of the pilot as a personality."

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PRINCIPAL RESULTS OF RESEARCH IN BIOPHARMACY

Moscow FARMATSIYA in Russian No 4, 1977 pp 1-4

[Article by A. I. Tentsova, All-Union Scientific Research Institute of Pharmacy, Moscow]

[Text] Among the pharmaceutical disciplines, biopharmacy occupies a special place, not only because of the novelty of concepts on which it is based, but as a result of its importance to theory and practice of modern pharmacy.

Having emerged as a reaction to the merchandising direction of pharmacy, biopharmacy has no accumulated data that permit a scientific description of drugs from the standpoint of their behavior in the living organism.

The biopharmaceutical consideration of drugs and biopharmaceutical methods of evaluating their quality do not preclude former methods and standards, but view them as methods that determine the commercial properties of drugs.

In the time of its existence, biopharmacy has been enriched with new discoveries and has occupied a firm place in the system of modern pharmacy [drug science]. We can single out the following main directions of biopharmaceutical research, in which some results have obtained, both in the USSR and abroad: investigation of pharmaceutical factors; investigation of biological accessibility of products; development of methods and instruments to determine the latter; development of methods of demonstrating products in biological fluids; investigation of conditions of absorption, transport and elimination of products as related to variable factors of the internal and external environments.

More recently, studies have begun of the effects of age, biological rhythms, interaction of drugs taken simultaneously, composition of food on processes of drug absorption and metabolism. This does not exhaust by far the breadth of biopharmaceutical research, although it does reflect the vast spectrum of its scientific concerns.

Analysis of the research done in institutions under the jurisdiction of the "Pharmacy" Problem Commission of the USSR Academy of Medical Sciences, as well as the First All-Union Symposium on Biopharmacy, revealed that research is being pursued in our country in all of the main directions of biopharmacy.

The above problems are being worked on primarily at the All-Union Scientific Research Institute of Pharmacy, Scientific Research Institute of Antibiotics, Tbilisi Institute of Pharmacology, Khar'kov Scientific Research Institute of Chemistry and Pharmaceutics, the Pyatigorsk and Khar'kov pharmaceutical institutes, Leningrad Chemopharmaceutical Institute, and on the pharmaceutical faculties of medical institutes of Moscow, Ryazan', Vitebsk, L'vov, Zaporozh'ye, and others.

In view of the great importance of pharmaceutical factors in the ultimate evaluation of therapeutic effects of drugs, numerous biopharmaceutical and clinical studies have been made of the effects of the type and route of administration of a form of drug, nature and amount of vehicle ["secondary agent"], dispersion, etc., on stability, pharmacokinetics and therapeutic efficacy of products.

Long before the inception of biopharmacy, many researchers (including clinicians) pointed to the significant relationship between the pharmacotherapeutic effectiveness of some products and the form of the drug. However, it is only with development of refined analytical methods of demonstrating preparations in drug forms and particularly in biological fluids that precise quantitative data were obtained, indicative of the relationship between rate of absorption and concentration of drugs in biological fluids, on the one hand, and the type of drug form, on the other.

According to biopharmaceutical concepts, the drug form, with the aggregate of its properties, has a significant influence on the effect of the drug it contains.

Results obtained under experimental and clinical conditions have confirmed the role of the form of a drug with reference to a number of products referable to different chemical and pharmacological groups (hormones, antibiotics, salicylates, spasmolytics, phenothiazines and others).

Thus, a comparative evaluation of drug forms (powder, tablets, suppositories, solutions, rectal ointments) with amidopyrine, acetylsalicylic acid, ephedrine hydrochloride, euphylline, streptocid, sulfadimethoxine, ascorbic acid, prednisolone, vitamin K, etc., established a significant difference in rate of absorption and time of retention of these products and their metabolites in the organism. With regard to many of them, after administration in suppositories, drugs were demonstrable in biological fluids at an earlier time and in an adequate concentration, which held at a high level for a long time.

A study of the role of drug form and route of administration of teturam and insulin revealed that there was virtually no difference in rate of access and level in blood of patients following administration by injection and rectum. Anesthesiologists failed to observe severe side-effects after administration of teturam by rectum, although they do occur after injections.

When using fluoracizine [10-(β -diethylaminopropionyl)-2-trifluoromethyl-phenothiazine hydrochloride] in the form of solution, tablets and suppositories, maximum concentrations of the product in blood were demonstrated after intake by mouth.

The influence of drug form and route of administration on distribution of drugs in tissues, organs and cells was demonstrated on the example of the phenothiazines.

Several rational drug forms, which have earned a good name for themselves in clinical practice, were developed and proposed on the basis of experimental observations.

Many researchers proved the correlation between therapeutic efficacy of drugs and their stability, on the one hand, and the excipients used (fillers for tablets, bases for suppositories and ointments, corrective agents, etc.).

Thus, analysis of production of ointments with antibiotics and investigation of the effects of vehicles on their stability has made it possible to refine the technology of dibiomycin, polymixin, oxytetracycline and neomycin ointments, and in a number of cases the concentration of antibiotics was reduced by 3-4 times with retention of therapeutic efficacy. Use of cellulose ethers in zincundane and undecine ointments increased their efficacy and stability.

The concentration of sulfanilamides was higher in dialysates of ointments prepared on an absorption basis with a hydrogenation product of sunflower oil in dialysates of ointments containing anhydrous lanolin alcohols.

Analogous results, indicative of a correlation between rate and extent of liberation and absorption of products and form of base were also obtained with the use of suppositories. For example, a maximum concentration of sulfadimezine, when cocoa butter is used as the base, is found 4 h after administration of suppositories, this is found after the 2d h with the use of GKHM5T and PYa5T. A more stable level of sulfadimezine throughout experiments is also observed with the use of GKHM5T and PYa5T bases.

Faster release of sulfanilamides from tablets was observed when sugar and starch were used as vehicles, as compared to tablets containing talc.

Corrective agents (fruit syrups) retard absorption of a number of products (amidopyrine, sodium and potassium bromides, calcium chloride, magnesium sulfate and others).

All this made it possible to formulate requirements concerning excipients. Only those that provide for optimum expression of the range of pharmacological properties of a product can be used with it, and this is the unbending rule in biopharmaceutical research.

Biopharmacy considers the extent of pulverization, nature of crystalline structure (presence of polymorphism) and solubility to be the most important characteristics, when examining the physical state of a drug.

Serious importance had always been attributed to questions of pulverization [particle size]; however, attention was given primarily to the technological properties of the ingredients that were to be broken down. Biopharmacy has established that the rate and thoroughness of absorption of a drug, its concentration and retention time depend largely on particle size. Quantitative characteristics have been obtained of this correlation with regard to many sulfanilamide preparations, antibiotics, phenothiazine derivatives, hormones and others.

In recent years, many researchers have concentrated on a comparative study of technological processes and industrial [production] factors, in order to choose the optimum ones, from the standpoint of therapeutic activity and to assure therapeutic equivalence of drugs.

Thus, studies were made of the biological accessibility of sulfanilamide, antibiotic and salicylate tablets manufactured at different plants. In spite of the fact that the tablets manufactured at all of the plants met the GFKh [expansion unknown] specifications and contained the same amounts of the product, they varied significantly in biological availability.

The experimental data accumulated to date make it possible to use a basically new approach to pharmaceutical factors, with consideration of correlations in the manufactured drug between all its components and their aggregate influence on the efficacy of the drug. For it is not the former, but the drug itself that began to be considered responsible for the therapeutic response.

Consequently, in each instance of producing drugs, specific variable factors (vehicles, manufacturing methods, drug form, etc.) must be selected, with due consideration of their multifaceted influence on the activity and side-effects of the product, depending on the properties of the drug.

Quite recently, work was begun on problems of rational administration of drugs by mouth and effects of food components on absorption of drugs.

Thus, absorption of tetracycline is worsened with intake of food rich in iron salts; insoluble complexes are obtained as a result of interaction in the stomach between products of the tetracycline class and the calcium of foods.

Interaction of drugs, when taken simultaneously is an extremely important question, since there has been an increase, in recent years, in number of reports of interaction between drugs; cases have been described of altered efficacy, toxicity of interacting drugs and even fatalities.

Interaction between drugs and food and other drugs includes problems that must be solved with due consideration of physicochemical, biochemical, physiological and pharmacological patterns.

While the biopharmaceutical aspects of drug form and excipients have been supplied with rather profound theoretical substantiation and practical implementation, this cannot be said about problems of dispersion, polymorphism, interaction between drugs and food and other drugs in combined therapy. Work on these problems requires expanded and in-depth experiments.

Biopharmaceutical experiments require the use of special investigative methods in order to determine solubility, demonstrate products and their active metabolites in biological fluids, correlation between product level in blood and degree of clinical response.

The first stage of investigation of biological availability is to determine the solubility or time in which the product is released from the drug form. It has been established that, in the first approximation, the solubility test characterizes the biological availability of a product, since there is a rather frequent correlation, in practice, between rate of dissolution and absorption.

Results have been obtained that indicate the existence of a correlation between kinetics of absorption and rate and degree of dissolution of streptocid, acetylsalicylic acid, sodium salicylate and others in tablet and suppository form. It was found that the faster and more completely the substances are released, the higher their maximum concentration in blood. In spite of the importance of the solubility test, there is still no standard method or instrument for experimental determination of dissolution rate. Some attention is being given to development of methods of analyzing drugs and their metabolites in biological fluids.

More recently, questions of pharmacokinetics and mathematical modeling of absorption processes have been of great interest; without knowledge of these aspects it would be impossible to obtain correct results from research. However, involvement of many scientists is required to develop methods of studying biological availability of drugs and methods of quantitative analysis of products in biological fluids, since without them the pursuit of many biopharmaceutical investigations is held back. Solving all the problems set forth by biopharmacy goes far beyond the framework of pharmacy and involves primarily pharmacological and clinical experimentation. In this regard, it is imperative to conduct combined research on a wider scale. The demands presently imposed by the USSR Ministry of Health with regard to the drug forms being developed make it imperative to have such close relations with various specialists: comparative laboratory studies of disintegration of a product and passage into solution of active agent; comparative laboratory studies of the level of the active agent in blood at the absorption phase, with analysis of the curves obtained; investigation of acute and chronic toxicity of agents with a narrow range of therapeutic action (steroids, anticoagulants, antidiabetic agents, cardiac glycosides, antibiotics and others).

Thus, the development of biopharmacy involves a revision and reevaluation of traditional theses of pharmacy, rationalization of pharmaceutical technology, development of new methods to study drugs and development of rational drug forms.

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SPACE BIOLOGY

MEDICINE FOR PILOTS

Moscow NAUKA I ZHIZN' in Russian No 6, 1977 pp 130-131

[Article by Vladimir Fedorovich Tokarev, Head of the Medical Administration of the USSR Ministry of Civil Aviation]

[Text] Surprises at High Altitudes

Relatively recently, when aircraft began to fly at high altitudes, it was learned that not all food by far is beneficial to the pilot before a flight. For example, oranges harbor a danger, even though they are rich in vitamins. And it is not only oranges that are contraindicated for pilots; this may also apply to fresh rye bread, milk, bean soup, "okroshko" [cold kvass soup], kvass [a fermented drink] and, occasionally, even famous Pepsi Cola.

All this is quite simple to explain: the above-mentioned products cause somewhat increased gas formation in the course of digestion. Accordingly, there is elevation of intraabdominal pressure. In the usual atmospheric pressure, no one pays attention to abdominal distension; it is simply not noticed and brings no harm. But at low pressure, when the air is somewhat rarefied, a consumed orange could distend the intestine to such an extent that the latter, raising the diaphragm, would press on the heart and induce vasospasms. If something like this happens to a pilot while piloting an aircraft at high altitudes there could be unpleasant consequences.

Pilots' Regimen

In order to be prepared for such "irregular" situations, specialists in the field of nutrition have developed a diet for pilots, while physicians in aviation medicine have established a work and rest regimen for flight crews.

At a specific time before a flight, the crew goes to a prophylactorium for preflight rest and free food. All of the dishes are prepared with due consideration of the physiology of work in flight.

There is scientific substantiation of the work and rest regimen for pilots and strictly specified flight time standard, i.e., the number of hours that the crew spends in the air over a day, month and year. This regimen is a law.

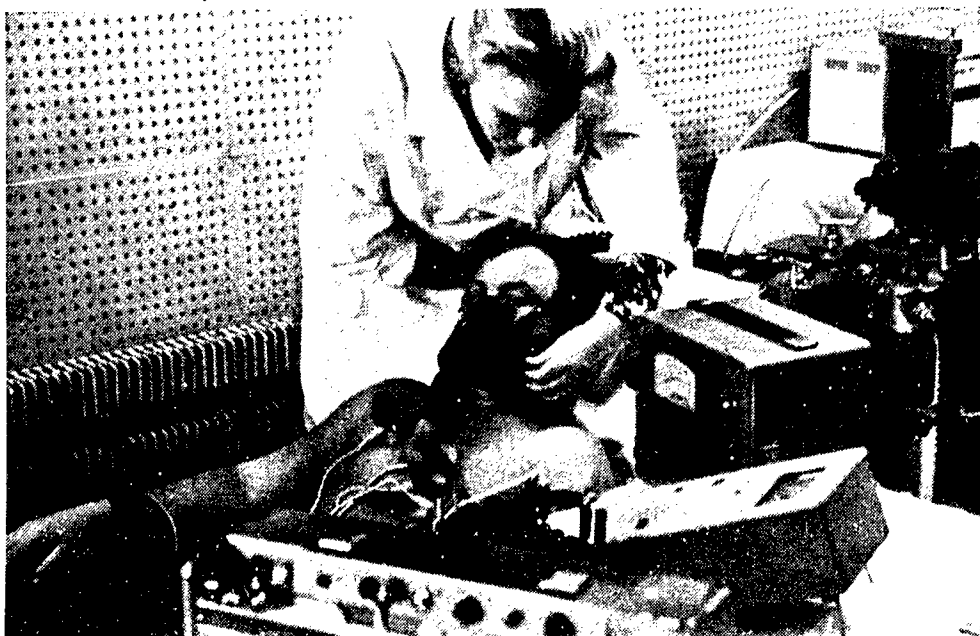


Figure 1.

Mikhail Bushuyev, commander of the Tu-154 craft, being checked "for hypoxia"; he is given a gas mixture to breath through a mask, with low oxygen level, as if he were at an altitude of 5000 m. There is also another method of "climbing": a pressure chamber, where the gas mixture and ambient pressure correspond to a specified altitude. If even minor health problems are present, the instruments that record the status of the organism would immediately call attention to them. Mariya Popkova, pressure chamber feldsher, is making the test.



Figure 2.

Clinicodiagnostic laboratory of the Central Aeroflot Hospital is equipped with the most refined equipment. The biochemical analyzer performs a biochemical blood test very rapidly and prints out results on 18 parameters. Such equipment is still a rarity.

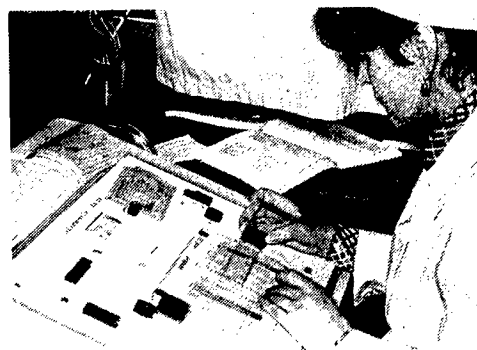


Figure 3.

A pilot must have perfect hearing. Hearing is tested with an objective instrument, an audiometer. The pilot is put in a soundproof chamber and puts on earphones, the instrument does the rest. Here, nurse Galina Yershova is monitoring the audiometer.



Figure 4.
Vladimir Chernomor, Tu-154 craft commander,
is tested on a bicycle ergometer. The
"mileage," time and speed are specified.

Some deviations of health status may appear with age and accumulation of many hours of flying time, which would be unnoticeable to an individual and do not affect work performance. Such deviations can be detected only by a medical specialist who supervises the pilot, and even then occasionally only with the help of instruments. If even the slightest impairment is observed, the pilot is immediately referred for treatment, including sanatorium care. And this procedure is followed faithfully.

Each pilot undergoes a comprehensive physical examination at very specific intervals, and civil aviation pilots are granted a paid leave twice a year.

In our country, the requirements with regard to pilots' physical condition are much higher than those of ICAO--the International Organization of Civil Aviation.

Pilot Eligibility

In the early days of aviation, a pilot had to be strong and in good health. With the advent of more complex craft, there was also an increase in requirements of pilot candidates. Today's high-speed aircraft, outfitted with many instruments, are literally "larded" with electronic equipment and have altered appreciably the nature of pilots' work. At the present time, by far not every young healthy individual is capable of performing such work, which involves an appreciable psychological load.

A young person enrolling in a flying school today must be not only in good health but also psychologically suitable; for this reason, those who enroll undergo a thorough screening by a psychologist. The objective of the screening is to evaluate occupationally important skills: rate of mental processes, rapidity of developing and altering intellectual skills, operational memory capabilities. Special tests have been developed and are used for this purpose. The psychologist [physician] also determines from the tests such important personality traits as perseverance, courage and ability to rapidly make a justified decision. But this is not the only function of the psychologist: he also supervises trainees and pilots with thousands of hours of flying time.

A Few Words About Physicians

The physician in aviation medicine is a physician in a special category with specific tasks; for this reason he undergoes special training. Such training is given on the chair of aviation and space medicine of the Central "Order of Lenin" Institute for Advanced Training of Physicians. The chair is headed by Prof G. L. Komendantov, laureate of the State Prize. It should be mentioned that, by special arrangement, specialists sent by foreign aircraft companies also undergo training on the same chair.

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SCIENTISTS AND SCIENTIFIC ORGANIZATIONS

VASILIIY NIKOLAYEVICH REMESLO

Kiev FIZIOLOGIYA I BIOKHIMIYA KUL'TURNYKH RASTENIY in Russian No 1, 1977
pp 105-107

[Article by P.A. Vlasjuk and I.V. Moroz: "Jubilee Dates -- Vasiliy Nikolayevich Remeslo (On the Occasion of His 70th Birthday)"]

[Text] Scientific society and agricultural workers of the USSR are celebrating the 70th birthday of the eminent scientist-plant breeder, Academician of the USSR Academy of Sciences and VASKhNIL [All-Union Academy of Agricultural Sciences imeni V.I. Lenin], Lenin prize laureate, Hero of Socialist Labor, honored scientific figure of the Ukrainian SSR and director of the Mironovo Order of Lenin Scientific Research Institute of Plant Breeding and Seed Production for Wheat, Vasiliy Nikolayevich Remeslo.

The work carried out by Remeslo serves as a bright example of tireless service in behalf of the nation and domestic science. This scientist has traveled a glorious path. His entire life has been devoted to carrying out very difficult and yet very necessary work -- the creation of new and highly productive strains of wheat. The theoretical principles and methods which he developed for plant breeding work and also the highly productive strains of winter wheat which he created are considered to be great international achievements and they represent an important contribution to the depository of domestic and international agricultural science.



Vasiliy Nikolayevich Remeslo was born into a peasant family on 10 February 1907 in the village of Teplovo, Piryatinskiy Rayon, Poltavskaya Oblast. Upon completing a program of study at the Maslovo Institute of Plant Breeding and Seed Production, he worked at the Derbent base of VIR [All-Union Scientific Research Institute of Plant Growing] and thereafter at the Novourensk (now Ul'yanovsk) and Severo-Donskaya plant breeding experimental stations. V.N. Remeslo began his scientific studies in the Volga region under the direction of the eminent specialist in experimental work, P.N. Konstantinov. His contacts with the well known plant breeders V.Ya. Yur'yev and A.A. Sapegin were of great importance with regard to his development as a scientist and plant breeder.

In 1948, by which time he already possessed a considerable amount of experience in carrying out scientific-research work, Vasiliy Nikolayevich transferred to the Mironovo Plant Breeding Experimental Station where he served as deputy director for scientific work and head of a plant breeding section. In 1964 he became the director of this station. In 1968 this plant breeding experimental station served as the foundation for the creation of the Mironovo Scientific Research Institute of Plant Breeding and Seed Production for Wheat. Academician Remeslo was appointed to serve as the director of this institute.

In 1956, Vasiliy Nikolayevich was awarded the scientific degree of Candidate of Biological Sciences and in 1964 -- Doctor of Agricultural Sciences.

V.N. Remeslo devoted all of his scientific work to the creation and introduction of new and highly productive strains of wheat into the operational practice of kolkhozes and sovkhozes. He bred winter wheat strains for the northern regions of the country and he developed breeding methods for obtaining strains having the desired economic characteristics.

By implementing improvements in and creatively employing the method of direct transformation of spring forms of wheat into winter forms, V.N. Remeslo succeeded in breeding more productive and winter hardy strains of winter wheat -- Mironovskaya 264, Mironovskaya 808 and others.

He made extensive use of the hybridization method. The strains obtained by means of strain and line transformations he crossed among themselves and also with strains having different genetic and ecological origins. It was established that hybrids created in accordance with this method are characterized by prolonged heterosis. Such material is particularly valuable for breeding work, as borne out by a number of strains bred by Remeslo. For example, Mironovskaya Yubileynaya and Il'ichevka have already been regionalized and are being planted over large areas. The former was obtained by means of a hybrid combination of Lyutetsens 106 (altered Artemovka) X Bezostaya 4 and the latter -- Bezostaya 4 X Mironovskaya 808.

The winter wheat strains Mironovskaya 808, Mironovskaya Yubileynaya and Il'ichevka, bred by V.N. Remeslo, have entered firmly into production operations and are being sown throughout our country on an area of approximately 10 million hectares, or approximately 40 percent of the entire area devoted to this particular crop. Those kolkhozes and sovkhoses which are employing these strains are annually obtaining 1.3-3.3 million additional tons of high quality bread grain. The economic effect realized from the introduction into production of the Mironovskaya 808 strain alone is expressed in terms of obtaining an average of 168.1 million rubles of additional income annually. In the Ukrainian SSR the additional income realized from the introduction of this strain into production during the Ninth Five-Year Plan amounted to 304.7 million rubles.

A typical characteristic of the strains created by Vasilii Nikolayevich is their great adaptability and ecological plasticity. This enables them to be cultivated successfully in various regions of the Soviet Union and in a number of foreign countries. For example, the Mironovskaya 808 strain has been regionalized and is being sown in 86 oblasts and krays in our country and also in Czechoslovakia, the GDR, Poland, Hungary and in a number of capitalist countries. These strains are furnishing high yields not only in the old and traditional regions in which winter wheat has been grown, but also in the non-chernozem zone of the RSFSR, the Baltic region, Belorussia, the Priural'ye region and in the Altay.

In recent years, Academician V.N. Remeslo has created a number of new and highly intensive strains of winter wheat -- Mironovskaya 10, Mironovskaya 808 (improved), Mironovskaya 11 and Mironovskaya 25. At the present time, these strains are undergoing state testing and checking at kolkhozes and sovkhoses located in various soil-climatic zones throughout the country.

The development by Vasilii Nikolayevich of the Mironovskaya Yarovaya spring wheat strain is considered to be a great achievement. It was obtained by transforming Mironovskaya 808 winter wheat into a spring form, using vernalized seed in a spring sowing. This strain, which furnishes a yield of 45-50 quintals per hectare, holds great promise not only for resowing and undersowing on damaged winter crop plantings, but also for sowing on spring fields. This will make it possible to increase the production of high quality bread grain, particularly in the Altay and in northern Kazakhstan.

V.N. Remeslo is carrying out diverse types of work associated with the creation of highly productive short stalk strains of wheat.

By means of strain testing carried out at nurseries, V.N. Remeslo is studying materials which differ in terms of their ecological and genetic nature and which will be used in the future for creating winter wheat strains having productivities of 90-100 quintals per hectare.

In the interest of developing more efficient plant breeding methods, basic studies were carried out at the institute, under the immediate direction of Vasiliy Nikolayevich Remeslo, for the purpose of studying the genetic and physiological-biochemical principles underlying the creation of highly productive forms of winter and spring wheat and triticale. As a result of these studies, the plans for which called for collaboration with other institutes of the Soviet Union and CEMA member states, extensive use will be made of the method which involves transforming spring forms into winter forms. Improvements were realized in other methods employed for breeding winter wheat strains possessing both high productivity and raised winter hardiness and capable of withstanding temperatures down to -23 degrees in the tillering zone area. The creation of such forms will make it possible to solve a very important problem associated with the introduction of winter wheat plantings in the eastern regions of the country, such as northern Kazakhstan and the Altay.

The implementation of improvements in seed production work occupies an important place in the work carried out by a plant breeder. Under the direction of V.N. Remeslo, a seed production system for grain and pulse crops which calls for all farms to be supplied annually with elite seed for their propagation plots was developed and introduced into operations. This system makes it possible to introduce new strains within the course of 1-3 years.

Vasiliy Nikolayevich has been a member of the CPSU since 1942 and he has carried out a great amount of social work. He has repeatedly been elected to serve as a member (he presently holds this post) of the Central Committee of the Communist Party of the Ukraine and as a deputy to the Supreme Soviet of the Ukrainian SSR. He is a member of the presidium and chairman of the Grain Crop Section in the Crop Husbandry and Plant Breeding Department of VASKhNIL. He performs a great amount of work in connection with furnishing scientific-methodological assistance to plant breeding centers throughout the country.

Academician V.N. Remeslo has authored more than 140 scientific works on such subjects as plant breeding, seed production and high quality agricultural practices for use in the growing of field crops.

The creative work performed by V.N. Remeslo over a period of many years has been valued very highly both by our country and by other foreign countries. He was awarded the Lenin Prize (1963) and also the Prize imeni Academician V.Ya. Yur'yev, the title of Hero of Socialist Labor (1966) was conferred upon him and he is an honored scientific figure of the Ukrainian SSR. In 1964, V.N. Remeslo became a member of VASKhNIL and in 1974 -- a member of the USSR Academy of Sciences and a corresponding member of the Agricultural Academy of the GDR. He is a member of the international organization Yeukarpiya.

For successes achieved in the agricultural field, V.N. Remeslo has been awarded many decorations: Red Banner of Labor, "Badge of Honor," October Revolution, the Order of Lenin on three occasions and also many medals.

For the contribution made by him towards increasing the gross yields of grain, V.N. Remeslo was awarded decorations by other fraternal socialist countries: "Labor" (Czechoslovak SSR), "Rebirth of Poland," "Gold Star of Friendship of the People of the GDR," "Banner 1st Degree" (Hungarian People's Republic).

Vasiliy Nikolayevich Remeslo is celebrating his jubilee in the prime of his creative strength and activity. We wish our dear friend further fruitful endeavors, great creative successes and good health.

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SCIENTISTS AND SCIENTIFIC ORGANIZATIONS

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CURRENT PRACTICES, PROBLEMS, GOALS IN UKRAINIAN MEDICAL EDUCATION

Kiev VRACHEBNOYE DELO in Russian No 4, 1977 pp 1-8

[Article by A. Ye. Romanenko, Ukrainian SSR Minister of Health: "Tasks of Further Improving Higher Education"]

[Text] The 25th CPSU Congress, a historic event in the life of our homeland, scientifically defined the realistic social-economic, ideological, and foreign policy strategy and policies of the party at the present stage; it gave the Soviet people an ambitious program of creative activity in all spheres of social development. A component part of this program is the course toward decisively improving the work of the health care system and enhancing the effectiveness and quality of higher education, the implementation of which must be contributed to by our country's higher medical schools, including the VUZ collectives of the Ukrainian SSR.

The medical VUZ's are called upon to prepare physicians who take firm world-view and political stands, dedicated to the cause of communism, Soviet patriots and internationalists who possess fundamental specialized skills and knowledge, competent organizers. Improving the quality of physician and pharmacist training to meet the standards demanded of them by socialist health care at the end of the 20th century is the main way to enhance the effectiveness of the higher medical schools in the Tenth Five-Year Plan. The republic's medical VUZ collectives, guided by the decisions of the 25th CPSU Congress and the 25th CP Ukraine Congress, have undertaken considerable efforts to enhance the quality of cadre training. At the present time, physician and pharmacist training in the Ukrainian SSR is provided in 15 medical institutes and in the medical department of Uzhgorod University. Some 53,500 students are being trained in 37 of the republic's VUZ departments.

In the past five years (1971-1976), the number of physicians in the Ukraine has risen from 26.3 to 32.0 per 10,000 population, and by the end of the Tenth Five-Year Plan it will reach 36.9. It may be considered, therefore, that the problem of physician training is being resolved successfully in terms of quantity. The main task of the higher schools during the Tenth Five-Year Plan is to improve the quality of specialist training. This

derives from the requirements of the 25th CPSU Congress, the October 1976 Plenum of the CC CPSU, L. I. Brezhnev's speeches there, and the laws passed by the USSR Supreme Soviet. The activities of all links in the medical VUZ's must be subordinated to the resolution of this vital state task.

Improved quality of physician and pharmacist training should be facilitated primarily by the rational selection, indoctrination, and placement of teaching cadres, systematic efforts to upgrade their qualifications, improvements in the training and indoctrinational process, organization of the process on a scientific basis, intensification of instruction, generally higher standards imposed both on students and teachers and their personal responsibility, development of the training-material base, and improvements in the system of selecting the best-prepared young people for VUZ enrollment.

The ministry and the medical VUZ's have done considerable work to improve the training of scientific-teaching cadres. Special attention has been focused on the selection and placement of the management cadres of the medical VUZ's. On the basis of in-depth analysis, the ministry has worked out a long range plan for strengthening the management stance of the institutes and departments. In the past four years, measures have been taken to strengthen VUZ management cadres. Efforts are continuing to study the effective reserve of management personnel and VUZ department directors. Some 62 persons have been included in the reserve for the posts of rector and vice-rector, from among the best-trained deans, party committee secretaries, and department directors, whose age, as a rule, is not over 45. Some of these persons constitute a prospective reserve not only for the VUZ's but also the ministry.

At present, the republic's medical VUZ's are staffed with an adequate number of highly qualified teachers. More than 600 departments employ 5,700 profesorial-teaching staff personnel, including 10 percent doctors of sciences and 56 percent candidates of sciences; 48 percent of the teachers are CPSU members. In some institutes (Kiev, L'vov), up to 75 percent of the teachers have scientific degrees and titles. Nowadays, no one doubts the necessity of training teaching cadres as a decisive factor in upgrading the quality of the specialists graduated by the VUZ's. This problem must always be at the focus of our attention, one of our most vital tasks. Teacher cadre training must proceed by way of systematic and goal-oriented efforts, which must be based on the principle of continuity and the alternation of generations while retaining and enlarging the scientific potential. More and more young people are now being drawn to teaching--a logical process, one which must be supported, developed, and provided with the necessary conditions for the growth of talented young people.

Special emphasis should be placed on the necessity of goal-directedness in the training of doctors of sciences: it must proceed in accordance with the needs for specialists of higher qualification in each specialty and realistic prospects for further utilization of the particular scientific-teaching worker.

It must be stated that the medical VUZ's have slackened in their work with graduate student training. This is indicated, in particular, by the decline, in recent years, of the number of graduate students who complete their dissertation work on time as stipulated by the plan. It is also necessary to focus serious attention on the organization and conduct of enrollment in graduate studies. Even today there are still cases in which there is essentially no competition: there is one application per place. The absence of competition for enrollment in graduate study and the lack of opportunity to select the most worthy of several candidates can hardly satisfy us.

In discussing the work of scientific-teaching cadre training, it is necessary to focus as well on the activities of the medical VUZ councils on dissertation defense. In past years, 11 medical institutes of the republic had 30 functioning qualified councils for awarding scientific doctoral and candidate of science degrees in 39 specialties of the medical, pharmaceutical, and biological sciences. The VUZ scientific councils have done considerable work in the certification of scientific and scientific-teaching cadres; this has helped in the shaping of the republic's high scientific potential.

At the same time, there have been serious shortcomings in the work of the councils with respect to scientific cadre training; they have brought it about that in the last few years the Higher Certification Commission turned down 17 doctoral and 17 candidate dissertations completed and defended in the scientific-medical institutions of the Ukrainian SSR: of these, nine were defended in the Donetsk, seven in the L'vov, six in the Odessa, three in the Kiev, and three in the Dnepropetrovsk medical institutes. At present, new specialized councils have been set up; higher standards are being imposed on their work. We must substantially raise the responsibility of the chairman and members of these councils, dissertation chairmen, and official and unofficial opponents for the quality of dissertation work completed; we must not allow any more substandard performance in this work which is so vital to cadre training. Responsibility for the organization and quality of these efforts rests primarily with the VUZ managers.

One of the main directions in VUZ activity with regard to enhancing the quality of physician cadre training is the scientific organization of the training process. A physician graduated by a VUZ should meet the highest standards of our time. A great deal has been done toward improving and organizing training-educational work in the republic. The activities of the institute collectives in recent years have been directed toward improving all types of scientific-methodological work, toward optimizing the training process on the basis of progressive ideas developed by the country's leading scholars. These issues have been discussed at scientific-methodological conferences held in the republic to deal with problems of optimizing the training process. They have touched upon general principles of organizing the training process, issues having to do with the unity of training and indoctrination, the adoption of programmed instruction

and supervision of student knowledge, the graphicness of the teachings, study of the students' time budget, organization of their independent work, and so on.

It must be emphasized, however, that within this substantial and vital VUZ work a comparatively small proportion has to do with problems of the scientific formulation of the organization of the training-indoctrinational process to set up pedagogical experiments and investigate the effectiveness of new forms and methods of teaching. Yet the possibilities here are immense. Above all, VUZ collectives must continue efforts in regard to revising and perfecting curricula, setting up interdepartmental programs and "integral process" methodological recommendations in connection with the adoption of new curricula.

Another, no less vital issue that must be dealt with is highly-qualified selection of information. The increase in the flow of information on each subject, given the limited amount of time, requires a thoroughgoing and goal-oriented selection of information, taking account of optimal volume. In the selection of information, it is especially necessary to take that which is already firmly established and recognized in science. A vital aspect of department work must be the development of information sources, including scientific substantiation of the number of lecture and practical hours, the development of training aids, the issuance of new textbooks and procedural aids for practical studies, the publication of courses of lectures reflecting the experience of teaching in a particular department, the development and rational utilization of technical means for transmitting information and visual aids (tables, transparencies, training films, training equipment, and so on). No less vital is the task of further studying the students' time budget, scientific formulation of the principles governing the students' independent work, including studies outside the auditorium.

At present, the main guiding principle in specialist training is to teach the student to acquire new knowledge on his own on the basis of fundamental information--that is, to train him to work creatively. In his speech on 19 October 1971 at the All-Union Student Rally, L. I. Brezhnev stated: "Yes, the main purpose of the student is to learn...To thoroughly and completely master the programmed material of the VUZ is essential. But this alone is not enough. It is essential to learn how to refine one's knowledge constantly, to develop the skills of the researcher, a broad theoretical viewpoint...

"The teaching process in the VUZ today is based more and more on the student's independent activities, activities approximating research."* In these statements, Comrade L. I. Brezhnev precisely emphasized the new demands imposed on the specialist; these must be reflected in the organization of the training process in the VUZ's.

*L.I. Brezhnev, "Leninskim kursom. Stat'i, rechi" [On Lenin's Course. Articles, Speeches], Moscow, Politizdat, 1972, Vol 3, pp 428-429.

Today we can consider full-fledged only the kind of specialist who is capable of finding solutions to new situations--possessing high creative capabilities. Consequently, the goal in physician training is shifting away from attempts to equip the student with a maximum of actual data and toward the greatest possible development of his creative capabilities. This work must proceed from the very first day the student spends in the institute. The VUZ must set up a system in which each student goes through a school of independent creative activity during his training period. These problems can be resolved most adequately by incorporating scientific-research work into the training process; this will help to instill more deeply the theoretical knowledge acquired by the students in their studies of the disciplines of the curriculum, the development of high standards they impose on themselves, precision, accuracy, and scientific objectivity; it will enhance every student's opportunity to acquire the skills of the researcher within the walls of the VUZ. Much has already been done along these lines in recent years. A number of VUZ's (Kiev, Dnepropetrovsk, L'vov, Donetsk, and others) have introduced elements of scientific work in the curricula, extensively recruiting students for ongoing research. This has unquestionably already exerted substantial influence on specialist training. We must admit, however, that we are still far from a complete solution to the formulated task. In the next few years, every institute will have to introduce into the teaching process elements of student scientific research; they will have to substantially expand the implementation of training-research and scientific-research work and revise courses to incorporate these requirements. It is essential to find a complete solution to one task which is vital in the present-day higher school system--to make science an effective form of instruction.

Improving and intensifying the training process in the VUZ, one of the bases for enhancing the quality of specialist training, requires an accurate solution to problems of organizing control of the current success rate of the students. Since September 1974, all the medical VUZ's in the Ukraine have introduced the practice of intermediate academic certification of students; this takes place three times per semester and six times during the academic year. The experience acquired so far indicates that this is undoubtedly a progressive form of control in the training-indoctrinational process, one which helps to enhance the responsibility of both the students and the teachers. At the same time, there are a number of shortcomings in the way it is conducted: frequently the departments take a purely formal approach to the certification of student work; sometimes, the certification results are not adequately analyzed and brought to the attention of all students; certain departments sometimes do nothing at all by way of analyzing the results of certification and, consequently, do not map out specific measures designed to improve the quality of the instruction. It must be emphasized that the VUZ's will have to do a great deal of work to perfect the certification system, to take steps to precisely organize the system of analyzing its results and to map out specific measures in each case to improve the quality of training-indoctrinational work on all levels--the academic group, course

work, the department, the faculty, the rectorate, and the institute as a whole. There is serious cause for alarm in the fact that four percent of the students are getting grades of "satisfactory"; the figure is 8.2 percent at the Zaporozh'ye Institute and 5.2 percent at the Voroshilovgrad Institute. We can hardly expect that such students will turn into good specialists. The low success rate is the main factor in why students are dismissed from the institutes.

Substantial and responsible tasks face the collectives of the medical VUZ's in connection with the conversion to the new curriculum this year; this requires a substantial restructuring of the training process. It involves definite difficulties, but we will have to resolve the task in the next two years. One of the thrusts in methodology work can and must be a study of the principle governing the structuring and systematics of medical courses. In this regard, special attention must be focused on studying problems of continuity in the teaching of individual disciplines covering the entire course of study. In order to improve the quality of the organization of the training work in our VUZ's it is essential to undertake a scientific formulating of network training plans, the development of integral process programs of exposition of individual diseases in different departments, thus eliminating unnecessary duplication. One other, very vital aspect of the work is the task of perfecting teaching methodology. The experience of teaching theoretical and clinical disciplines has demonstrated the advisability of making extensive use of programmed teaching and controlling student knowledge, using both machine and conventional methods.

As is well known, at present all of the republic's medical VUZ's are training physicians through the subordination and internship. The primary specialization has required substantial restructuring of the entire training process in the VUZ, and a great deal has been done in this regard. Specialization in the subordination and internship provides good opportunities for the initial training of qualified specialists and to a greater extent meets the requirements of practical health care. The role and significance of primary specialization of the graduates of medical institutes are difficult to overestimate. On the one hand, it has made it possible to substantially enhance the professional training of the graduate; it has made it possible to conduct the training in a directed fashion, or, to put it in the language of technology, with final polishing at the stage of completion; on the other hand, it has constituted an excellent stimulus for upgrading the quality of the work of many practical medical treatment institutions. The medical institutes must focus more attention on selecting the internship bases, the selection and upgrading of qualifications of intern directors, systematic supervision and control over the progress of intern training.

A special place in the primary specialization (as, indeed, during all the time the student spends in the VUZ) must be given to the task of mastering practical skills. Considerable discussion, many speeches, and resolutions have been devoted to this problem. The situation has improved somewhat,

but it must be admitted that even today's graduate does not adequately possess all the skills that are so essential to the present-day physician. It is becoming perfectly clear that it is essential to establish precise quantitative indicators on the types of practical skills and the degree of their mastery in the process of VUZ instruction (such a study has been made in several institutes). If, moreover, this principle is also extended to the sphere of theoretical training and indoctrination, it will be possible to determine an optimal characterization of the graduate with regard to the defining parameters—that is, the standard or model of the specialist. By comparing standard indicators with actual findings it will not be difficult to evaluate the level of success of the training of the graduate in quantitative terms. In consideration of the above, it is essential to urge key departments, teachers, scientists, and methods specialists to step up the formulation of the model graduate with regard to each specialty.

Among the tasks assigned to the higher school by the historic decisions of the 25th CPSU Congress and the decree of the CC CPSU and the USSR Council of Ministers "Measures to Further Improve Higher Education in the Country," a prominent place is assigned to the task of inculcating future specialists with a communist world view. Implementation of this task requires further improvements in the teaching of both the social and the special disciplines; it requires strengthened indoctrinational and methodology orientation in the teaching of all institute departments. The task of shaping a scientific communist world view can be resolved successfully in the medical VUZ provided that there is a creative alliance between the social science departments—especially the department of philosophy and scientific communism—and the departments of clinical and scientific profile, with the latter paying constant attention to methodology problems in modern science. The inculcation of the communist world view in student doctors represents a complex and multi-componential process. It is based on the study of the theoretical heritage of the Marxist-Leninist classics, the historic decisions of the CPSU and the Soviet state, the documents of the international communist movement, and the assimilation of programmed material in the social sciences. Its most important task is that of instilling in the students the ability to utilize world-view principles as a method of mastering their specialty, to resolve problems of medical practice and Soviet health care.

Subordinated to the task of the students' creative mastery of fundamental world views is that of teaching the social sciences in conjunction with fundamental problems of modern biological and medical science and Soviet health care practice. Also subordinated to this task is the methodological orientation of the teaching of specialized natural, medical, clinical, and hygienic disciplines, an orientation which consists of the application of world-view principles in order to correctly resolve problems of medical science and medical practice.

The methodological orientation of the teaching also incorporates criticism of idealistic and metaphysical currents in modern medicine and health care theory abroad. Every department must determine, in accordance with the

characteristics of its subject matter and course program, the range of problems to be elucidated in lectures and practical studies. In accordance with the above considerations, it is essential that every department draw up a well thought out, methodical, efficient system of operations with regard to the methodological orientation of course teaching.

The link which connects all aspects of life in the VUZ is the ideological-indoctrinational work. New, higher standards are being imposed on it now.

In addition to professional skills, the graduate of a medical VUZ must possess the ability to correctly evaluate and elucidate issues in the domestic and foreign policies of the CPSU and the Soviet state; he must be able to prepare lectures and discussions on social-political and social-economic subjects; he must be able to conduct a meeting--that is, he must possess organizational skills and act as a vehicle conveying the party's policies to the masses. The social-political training of the students should promote this. Such practice is designed to deepen their knowledge, to promote the development of social-political involvement, inculcation of a creative attitude toward their future profession, the ability to organize their work and the work of the collective to resolve specific political, economic, and social tasks. For this reason, problems of the organization and conduct of social-political practice must be kept in mind by all teachers.

The third labor semester has come to be acknowledged as a school of communist indoctrination for the students. It has become firmly entrenched in the life of the VUZ's and has become an inseparable part of the training-indoctrinational process, a school of social-political and labor toughening. At the All-Union Students Rally, CC CPSU General Secretary Comrade L. I. Brezhnev said that student construction detachments "...constitute a form for opening up and mobilizing student energy, student commitment, which, in my opinion, completely meets the requirements of our times, as well as the needs of young people themselves. Participation in student construction detachments sows good seeds in the hearts of young people, seeds which produce beneficial yields."*

Last summer, 9,300 students of medical institutes took active part in student construction detachments; these detachments utilized about 17.7 million rubles in capital investments. More than 13,200 staff members and student doctors took part in agricultural work, completing work volumes in the amount of more than 600,000 rubles. Students also made a substantial contribution in the work of preventive treatment institutions. About 1,300 students worked in them as orderlies and junior nurses, and this form of student labor must be developed constantly, tying it in with the needs of practical health care. The patriotic movement "Students in Public Health Care" is a relatively recent one, but we can already speak of its great significance both for health care and for the students themselves.

*Ibid., p 432.

A vital component part of ideological work is indoctrination in internationalism. Since 1960, five VUZ's have trained specialists for 82 foreign countries, constituting a total of about 2,000 students. In 1976 alone, more than 500 foreign citizens were accepted for enrollment, and their number should increase every year. For this reason, the rectorates and party and Komsomol organizations of the VUZ's face the vital task of indoctrinating and training them in the spirit of friendship and respect for the socialist system, in the spirit of genuine internationalism.

All ideological-indoctrinational work in the VUZ must be based on decisions of the 25th CPSU Congress and the 25th CP Ukraine Congress. Rectors and party and social organizations in the medical VUZ's must systematically perfect all forms of ideological-indoctrinational work among the students; they must enhance its effectiveness. It must be kept in mind that indoctrinational work must be designed not only for the student body mass as a whole--it must also be individual, getting down to the level of each student.

The students' main teacher, educator, and mentor, the person who imparts not only knowledge but also his life experience, culture, character traits, ideological convictions, and dedication to the cause of communism--is the instructor--the professor, the docent, the aide. Enhancing the role and responsibility of the departments and their party groups for the communist indoctrination of the students is the main link in cadre training. The departments play a key role, because it is they who come into daily contact with the students; it is there that the pedagogical and science cadres are concentrated and shaped organizationally. This applies to all departments without exception, as was specially emphasized by CC CPSU Politburo member and CC CP Ukraine first secretary V. V. Shcherbitskiy in his speech at the Kiev State University imeni T. G. Shevchenko in October 1973: "The task of student training and indoctrination can be resolved only through the joint efforts of representatives of all sciences." Every department must find the most effective means of shaping the present-day specialist, on the basis of the specifics of its science, coordinating its efforts with other departments, especially in the field of instilling in each student an inner psychological attitude toward learning. It is the teachers of the departments who create an appropriate psychological micro-climate in academic groups.

It must be emphasized that in the matter of enhancing the quality of specialist training and indoctrination, substantial importance also attaches to the overall procedures of the training institution, the atmosphere of creative cooperation and commitment to the success of the work of one's co-workers and students, compliance with the "Standard VUZ Regulations." In connection with this, special emphasis must be placed on the urgent necessity of strengthening labor discipline among teachers, staff members, and students, enhancing the sense of responsibility for one's assigned task, strict supervision over the utilization of study time in all disciplines, also the necessity of uncompromising struggle against absenteeism and missing classes and lectures.

Within the limits of a journal article it is impossible to lay out in detail the tasks facing VUZ collectives in the next few years; only a few, general issues have been listed. Even these, however, testify to the necessity of substantially improving the effectiveness of institute work. Only in this way will it be possible to train specialists who can meet the high standards of Soviet health care.

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